

Botulism Guide for Health Care Professionals

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August 2022

This information requires knowledgeable interpretation and is intended primarily for use by health care workers and facilities/organizations providing health care including pharmacies, hospitals, long-term care homes, community-based health care service providers and pre-hospital emergency services.

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A Quick Response Guide to Botulism

Botulism – The treatment of botulism is guided by clinical diagnosis

The initial diagnosis of botulism should be based on a history of recent exposure, consistent clinical symptoms and elimination of other illnesses in the differential. Treatment should not wait for laboratory confirmation. All treatment and management decisions should be made based on clinical diagnosis.

Initial Presentation and evaluation of signs and symptoms

There are several clinically distinct forms of botulism. All forms produce the same neurological signs and symptoms of symmetrical cranial nerve palsies followed by descending, symmetric flaccid paralysis of voluntary muscles, which may progress to respiratory compromise and death. Additional symptoms (e.g., gastrointestinal signs in foodborne cases) may also be seen in some forms.

Reading the section on [Differential Diagnosis on page 6](#) and the referenced articles will assist with making the diagnosis of botulism.

Place a request for Botulinum Antitoxin (BAT) or BabyBIG®

Ministry of Health (ministry) staff will arrange for the shipment of BAT. Information on ordering BAT and BabyBIG (BabyBIG has a different ordering process) is on [page 10](#). As per the [BAT product monograph](#), there is a recommended dose for infants less than 1 year of age; due to lack of clinical evidence, the Ministry of Health supports clinicians in ordering requests for BabyBIG.

BabyBig® is only available through the California Department of Public Health and requires approval for use by [Health Canada's Special Access Program \(SAP\)](#). **It does not require ministry approval.** For more information on ordering BabyBig®, please see [page 11](#).

Laboratory Diagnosis and Specimen Collection

Clinical specimens should be obtained prior to administering treatment with botulinum antitoxin. Call the [Botulism Reference Service \(BRS\)](#) for Canada to make arrangements for transporting suspect food and clinical specimens to Ottawa for laboratory analysis.

Notify your local public health unit

Botulism should be reported even if it is only suspected and has not yet been confirmed. Information on the suspected food item should also be provided during the call.

Botulism

The initial diagnosis of botulism should be based on a history of recent exposure, consistent clinical symptoms, and elimination of other illnesses in the differential. Treatment should not wait for laboratory confirmation. All treatment and management decisions should be based on clinical diagnosis.

a) Initial Presentation and evaluation

There are several clinically distinct forms of botulism. All forms produce the same neurological signs and symptoms of symmetrical cranial nerve palsies followed by descending, symmetric flaccid paralysis of voluntary muscles, which may progress to respiratory compromise and death.^{*} Additional symptoms (e.g., gastrointestinal signs in foodborne cases) may also be seen in some forms.

Initially symptoms of foodborne botulism may include nausea, vomiting, abdominal cramps or diarrhea. Dry mouth, blurred vision, and diplopia are usually the earliest neurologic symptoms followed by dysphonia, dysarthria, dysphagia, and peripheral muscle weakness. These symptoms may extend to a descending symmetrical flaccid paralysis in an alert afebrile person.

^{*} Sobel, J., 'Botulism', *Clinical Infectious Diseases*, 2005, Vol. 41(8), pp. 1167-73.

Constipation is a common symptom later in presentation.

Wound botulism produces the same symptoms as foodborne botulism, except that, gastrointestinal symptoms, (vomiting and/or diarrhea) do not occur and neurological symptoms may take longer (up to two weeks) to appear.

In **infant botulism**, the earliest and most frequently observed symptom is constipation followed by lethargy, poor feeding, ptosis, difficulty swallowing, hypotonia and generalized weakness (floppy baby) including a weak cry.

Additional information assisting clinical diagnosis for infant botulism is available at the [Infant Botulism Treatment and Prevention Program website](#).

The symptoms observed in adult intestinal colonization botulism are similar to foodborne botulism. The clinical manifestation of iatrogenic botulism is similar to the characteristic findings seen in classic foodborne botulism, although nausea and vomiting are not typically present. Although inhalational botulism is not a naturally occurring disease, the syndrome was described once among laboratory workers in 1962, with symptoms resembling those of foodborne botulism. Please see [Appendix 1 Botulism: Clinical Description for additional information on symptoms and incubation period](#).

b) Differential Diagnosis

Differential diagnosis of botulism can be challenging because the symptoms mimic those of other diseases, especially diseases characterized by muscle weakness.

Botulism in adults must be differentiated from diseases such as the following: Guillain- Barré syndrome (GBS) (including the Miller Fisher variant of GBS), Myasthenia gravis, Lambert-Eaton myasthenic syndrome (LEMS), stroke or central nervous system (CNS) mass lesion, toxic exposures (organophosphates, atropine, carbon monoxide, or aminoglycosides), tick

paralysis, paralytic shellfish poisoning, and puffer fish ingestion.[†]

Botulism in infants must be differentiated from diseases such as the following: sepsis, meningitis, electrolyte-mineral imbalance, Reye's syndrome, congenital myopathy, Werdnig-Hoffman disease, and Leigh disease.[‡]

c) Laboratory Diagnosis

Laboratory testing to confirm the initial diagnosis can take at least 72 hours to complete and involves demonstrating the presence of botulinum toxin in serum, feces, gastric contents, vomitus or the implicated food; demonstrating toxicity to mice; or isolating *C. botulinum* from fecal specimens.

In wound botulism, *C. botulinum* may be isolated from a wound specimen.

For further information on the collection and transportation of suitable suspect food and clinical specimens please see *Appendix 2, Suitable Specimen Collection and Transportation*. More information regarding the process for sending samples to the BRS Laboratory can be found in Health Canada's [Botulism – Guide for Healthcare Professionals, 2020](#).

If botulism is suspected please contact the Botulism Reference Service (BRS) for Canada at **(613) 957-0902** (Monday to Friday; 8:30 a.m. – 4:30 p.m.). BRS will provide direction on the collection and transportation of suspect food and clinical specimens to Ottawa for laboratory testing which can also be found on the [Botulism Reference Service website](#).

d) Antitoxin use and clinical management

For all types of botulism, accessibility to respiratory support is essential; Supportive care combined with the rapid administration of botulinum

[†] Anderson, I.B., & Kim-Katz, S.Y., 'Botulism: Diagnosis and Management in the United States: A clinical and epidemiologic review', *Annals of Internal Medicine*, 1998, Vol. 120(3), pp. 221-228.

[‡] Ibid.

antitoxin (or immune globulin) is crucial to the successful management of botulism.

Supportive care combined with the rapid administration of botulinum antitoxin is crucial to successful management of botulism. Advice on the most up-to-date treatment should be sought from a clinical expert.

If feasible, prior to administering any anti-toxin, please ensure that serum from 20 mL of blood collected before administration of antitoxin is available to be shipped to the Botulism Reference Service for analysis. **Please note, the collection of serum is only applicable if it does not delay administration of antitoxin.** See [Appendix 2](#) for further information.

There are two types of botulism antitoxin:

1) Botulism Antitoxin Heptavalent (BAT):

BAT is indicated for the treatment of wound and foodborne botulism. The BAT product currently available in Ontario is Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G)-(Equine), which is approved for use against botulism in all age groups. BAT is obtained from horses immunized with the toxins of *C. botulinum* Types A, B, C, D, E, F, and G. The antibodies react specifically with and neutralize circulating botulism toxins (i.e., neurotoxin that is not already bound to neurons).

Antitoxin prophylaxis for individuals who do not display symptoms consistent with botulism is not recommended due to the risk of serum sickness and hypersensitivity reactions associated with antitoxin administration. Testing for hypersensitivity, as well as desensitization if the test is positive, against the product should be performed prior to administration of the product as per [manufacturer's instructions](#).

For wound botulism, in addition to antitoxin, the wound should be debrided and/or drainage established, and appropriate antibiotics (e.g. penicillin) administered. Attempts may be made to remove contaminated food still in the gut by inducing vomiting or by using enemas.

In accordance with the product monograph, one vial of BAT should be

administered to adults (> 17 years), 20-100 % of adult dose in children ≥ 1 year of age, and 10% of adult dose in children < 1 year of age, as soon as possible, on the basis of clinical diagnosis and **without awaiting laboratory confirmation**. Please refer to the [product monograph for BAT Heptavalent](#) for further dosage and administration details. Antitoxin is effective in reducing the severity of symptoms, if administered early in the course of the disease; however, it will not reverse established paralysis.[§]

Please refer to the product monograph for [Botulism Antitoxin Emergent BioSolutions®](#) for further dosage and administration details.

Note for pediatric populations: The recommendation for considering the use of equine antitoxin when BabyBIG® is not available or not indicated (i.e., non-type A or B infant botulism) would need to be handled on a case-by-case basis. Please consult the product monograph and the infectious disease specialist in your organization.

2) Botulism Immune Globulin (BabyBIG®):

Botulism Immune Globulin, Intravenous (BIG-IV); (BabyBIG®), is a preparation of human- derived botulinum antitoxin antibodies indicated in the treatment of infant botulism caused by toxin type A or B for infants up to one year of age.” BabyBIG® should be administered as a single intravenous infusion as soon as the clinical diagnosis of infant botulism is made. Please refer to the [product monograph for BabyBIG®](#) for further dosage and administration details.

Note: For more information regarding live vaccines not indicated following receipt of BabyBIG®, please see: [Package Insert - BabyBIG \(fda.gov\)](#), page 10.

[§] Wenham, T., & Cohen, A., 'Botulism', *Continuing Education in Anaesthesia, Critical Care & Pain*, 2008, Vol. 8(1), pp. 21-25.

” Fox, C.K., Keet, C.A., & Strober, J.B., 'Recent advances in infant botulism', *Pediatric Neurology*, 2005, Vol. 32(3), pp. 149-154

Process for ordering Botulinum Antitoxin (BAT) or BabyBIG®

Before placing an order for Botulinum Antitoxin (BAT) or BabyBIG® it is essential that you read the following sections within this guide:

- a) initial presentation and evaluation;
- b) differential diagnosis;
- c) laboratory diagnosis; and
- d) antitoxin use and clinical management.

Step 1: Place A Request for Botulinum Antitoxin (BAT) or BabyBIG®

1 a) Placing a request for BAT

A limited supply of BAT is kept on-site at the Ontario Government Pharmaceutical and Medical Supply Services (OGPMSS). Ministry staff will arrange for the shipment of BAT. Advice on administration is detailed in the product monograph which accompanies BAT. The ministry staff will advise OGPMSS of the authorization. The physician's information (i.e., name, address and phone number) will be provided to OGPMSS and they will prepare for the delivery of BAT.

Contact the ministry to place a request for BAT:

- **During Regular Work Hours** (8:30 a.m. – 4:30 p.m. Monday to Friday): Call the Infectious Diseases Policy & Programs Unit of the ministry's Office of the Chief Medical Officer of Health, Public Health at (416) 327-7392 and request to speak with a staff member.
- **After-Hours, Weekends and Holidays:** Call 1-866-212-2272 to retrieve the contact information for the on-call person.

Please provide ministry staff taking the order with:

- a) the name of the physician to whom the antitoxin should be sent
- b) the address to which the antitoxin should be sent
- c) the physician's contact telephone number

- d) the name of the public health unit in whose geographic jurisdiction the hospital is located.
- e) the last name of the patient

Please see Appendix 3 for summary of [process for ordering BAT or BabyBIG®](#)

1 b) Placing a request to access BabyBIG®

BabyBIG® is not approved for sale in Canada and can only be accessed from the Infant Botulism Treatment and Prevention Programs (IBTPP) at the California Department of Public Health (CDPH) by placing a request with Health Canada's [Special Access Programme \(SAP\)](#). The SAP will then authorize the CDPH to ship BabyBIG® to the hospital. The receiving hospital is responsible for paying the required fee to CDPH for BabyBIG®, as well as paying the transportation cost for BabyBIG® from California. The ministry will reimburse these costs upon receipt of the invoice. The [Special Access Request Form A](#) can be downloaded from Health Canada's website. Additional information on BabyBIG® can be obtained at the [IBTPP website](#).

Note: The current SAP process requires a clinical rationale as to why the drug being requested is indicated over a product that has already been licensed for use in Canada. Based on expert recommendations from pediatric infectious disease specialists, and in alignment with recommendations from other jurisdictions in Canada and internationally, Ontario supports the prompt initiation of BabyBIG® treatment in cases under one year of age with confirmed or strong clinical suspicion of infant botulism. BabyBIG® has demonstrated safety and effectiveness in treating infant botulism.

Place a request for BabyBIG® via Health Canada's SAP:

- **During Regular Work Hours** (8:30 a.m. – 4:30 p.m. Monday to Friday): The physician should fax the completed *The Special Access Request Form A* to the SAP at (613) 941-3194. To avoid delays all sections of the form should be completed accurately. It is recommended to follow up with a phone call to (613) 941-2108.

- **After-Hours, Weekends and Holidays:** The physician should call the SAP on-call officer at (613) 941-2108 (press 0). The attending physician should be prepared to provide the information required on the *Special Access Request Form A* to the on-call officer. On the next business day, the physician should fax the completed The Special Access Request Form A to the SAP at (613) 941-3194.

Call on-call physician at IBTPP to discuss the patient's clinical situation:

- Anytime, 24 hours a day, 7 days a week: Access to BabyBIG® is authorized only by one of the IBTPP on-call physicians. The patient's attending physician must call the IBTPP on-call physician at 1-510-231-7600 to discuss the clinical situation before BabyBIG® can be shipped.

Notify the ministry of the request for BabyBIG® from Health Canada:

- **During Regular Work Hours** (8:30 a.m. – 4:30 p.m. Monday to Friday): Call the Infectious Diseases Policy & Programs Unit of the ministry's Office of the Chief Medical Officer of Health at (416) 327-7392 and request to speak with a staff member.
- **After-Hours, Weekends and Holidays:** The attending physician should call 1-866-212-2272 to retrieve the contact information for the Office of the Chief Medical Officer of Health on-call person.

Please see Appendix 3 for summary of [process for ordering BAT or BabyBIG®](#)

Step 2: Collect and Make Arrangements for Transporting Suspect Food and Clinical Specimens to Ottawa for Laboratory Analysis

Collect and store appropriate food and clinical specimens as soon as botulism is suspected. Call the Botulism Reference Service (BRS) for Canada to make arrangements for transporting suspect food and clinical specimens to Ottawa for laboratory analysis:

- During Regular Work Hours (8:30 a.m. – 4:30 p.m. Monday to Friday): Call the BRS office at (613) 957-0902 prior to sending suspect food and clinical specimens to Ottawa for laboratory analysis.
- Samples should be sent by courier (do not use Canada post) to:

Dr. John W. Austin or Mr. Greg Sanders Botulism Reference Service
Health Canada
Room 456, Sir Frederick G. Banting Building 251 Sir Frederick Banting
Driveway
Tunney's Pasture, PL2204E
Ottawa, ON, K1A 0K9
- Specimens are not processed at BRS after work hours. Do not ship specimens to BRS after work hours without first consulting with the BRS office.

Please see [Appendix 2 Suitable Specimen Collection and Transportation](#) for basic information on the collection and transportation of suitable suspect food and clinical specimens. Health Canada's guidance on the collection and transportation of samples can also be found on their website under the [Botulism Guide for Health Care Professionals](#).

Step 3: Notify Your Local Public Health Unit Immediately

Botulism is a reportable disease in Ontario under the Health Protection and Promotion Act (HPPA) and must be reported immediately to the local medical officer of health by [telephone](#). The disease should be reported even if it is only suspected and has not yet been confirmed. Information on the suspected food item should also be provided during the call.

Appendix 1: Botulism – Clinical Description

Symptoms

Foodborne Botulism

Foodborne botulism is caused by the ingestion of food contaminated with preformed botulinum toxin and subsequent absorption of toxin through the gastrointestinal tract. Initially symptoms of foodborne botulism may include nausea, vomiting, abdominal cramps or diarrhea. Dry mouth, blurred vision, and diplopia are usually the earliest neurologic symptoms followed by dysphonia, dysarthria, dysphagia, and peripheral muscle weakness. These symptoms may extend to a descending symmetrical flaccid paralysis in an alert afebrile person. Constipation is a common symptom later in presentation.

Wound Botulism

Wound botulism is caused by toxin produced from a wound infected with the spores of *Clostridium botulinum*. The anaerobic conditions allow germination of the spores and production of toxin by vegetative bacteria that become systemically absorbed. This form of botulism produces the same symptoms as foodborne botulism, except that gastrointestinal symptoms (vomiting and/or diarrhea) do not occur and neurological symptoms may take longer (up to two weeks) to appear. Currently, the majority of wound botulism cases occur among injecting drug users who subcutaneously ("skin popping") inject street drugs contaminated with *C. botulinum* spores. Wound botulism may also occur following traumatic injury to an extremity, such as a compound fracture, laceration, puncture wound, gunshot wound, severe abrasion or crush injury. The presence of a wound is an important sign.

Infant Botulism

Infant botulism is caused by the ingestion of *Clostridium botulinum* spores, which then germinate in the intestine and produce bacteria that release toxin which is absorbed into the circulation. It affects infants under one year of age. The earliest and most frequently observed symptom is constipation followed by lethargy, poor

feeding, ptosis, difficulty swallowing, hypotonia and generalized weakness (floppy baby) including a weak cry.

Adult Intestinal Colonization Botulism

Adult intestinal colonization botulism is a very rare kind of botulism that occurs among adults who have anatomical or physiological abnormalities of the gastrointestinal system (i.e., intestinal surgery, inflammatory bowel disease or recent antibiotic treatment). The pathogenesis of this type of botulism is similar to that of infant botulism. It is caused by the ingestion of *Clostridium botulinum* spores, which then germinate in the intestine and produce bacteria that release toxin which is absorbed into the circulation. The symptoms observed are similar to foodborne botulism.

Iatrogenic Botulism

Iatrogenic botulism is caused by accidental overdose of botulinum toxin and has been reported in patients who have been treated with intramuscular injections of botulinum toxin for therapeutic or cosmetic reasons. Clinical manifestations are similar to other forms of botulism.

Inhalational Botulism

Inhalational botulism does not occur naturally. To date, only three human cases have been reported: this occurred in 1962 with veterinary laboratory technicians in Germany who were working with aerosolized botulinum toxin in animals. Symptoms occurred about 72 hours after exposure. This form of botulism is caused by inhalation of aerosolized preformed botulinum toxin with subsequent absorption through the lungs into the circulation.

Routes of exposure

Botulism is caused by exposure to botulinum toxin. Humans can become infected by:

Oral

Consumption of toxin – Foodborne botulism is a severe intoxication resulting from ingestion of preformed toxin of the bacterium *C. botulinum* present in contaminated

food.

Consumption of *C. botulinum* spores – Infant botulism and Adult intestinal colonization botulism results from ingestion of *C. botulinum* spores that then germinate in the colon, rather than by ingestion of preformed toxin.

Parenteral

Contamination of a tissue with *C. botulinum* spores – Wound botulism results from toxin produced from a wound infected with the spores of *C. botulinum*.

Contamination of a tissue with toxin – Iatrogenic botulism is the most recent man-made form of botulism that occurs due to infection of a large dose of toxin.

Inhalation

Inhalation of toxin – Inhalational botulism does not occur naturally, however, aerosolised toxin could be a potential route for infection as a result of deliberate release by bioterrorists.

Incubation Period

In foodborne botulism, symptoms generally begin 12 to 36 hours after eating a contaminated food but can also occur as early as six hours or as late as 10 days. The incubation period of wound botulism is longer, averaging about 10 days. The incubation period of infant botulism and adult intestinal colonization botulism is unknown.

Appendix 2: Suitable Specimen Collection and Transportation

Food samples may include leftovers or unopened containers. When commercial foods are involved, it is important to retrieve the label, the manufacturer's lot number and codes embossed on the can or package.

Suitable clinical specimens for analyses include:

- Fecal samples (approximately 10 g),
- Enema fluid,
- Gastric contents (adjusted to approximately a pH of 6.0 with 1N NaOH, if possible),
- Serum (from 20 ml of blood collected before administration of antitoxin).
- When infant botulism is suspected, the essential material for analysis is the infant's feces. As constipation is a common symptom, the following samples may be submitted if necessary: soiled parts of diapers, a rectal swab, 2 ml of serum or a combination of samples may be submitted.

Specimens should be handled according to routine practices and additional precautions and packaged for transport to the BRS, during work hours. After collecting the sample, but prior to shipping, ensure that the sample is stored in the refrigerator at approximately 4°C. For safe shipment, the specimens must be in a watertight primary receptacle, in a watertight secondary container, with sufficient absorbent material between the two containers to absorb the entire contents of the primary receptacle. The preferred method of preserving the material during shipment is by cooling rather than freezing, i.e., by including commercial cooling packs in the parcel. Before the specimen is shipped, inform BRS of the expected delivery date and time.

Appendix 3: Process for ordering BAT or BabyBIG®

Before placing an order for Botulinum Antitoxin (BAT) or BabyBIG® it is essential that you read the following sections within this guide:	<ul style="list-style-type: none"> a) initial presentation and evaluation; b) differential diagnosis; c) laboratory diagnosis; and d) antitoxin use and clinical management.
Step 1: Place a request for Botulinum Antitoxin (BAT) or Botulism Immune Globulin, Intravenous (BIG-IV); (BabyBIG®)	
Placing a request for BAT Obtain botulinum antitoxin from the Ministry of Health The ministry will direct processing and delivery of the antitoxin During regular work hours: (416) 327-7392 After-hours, weekends & holidays: 1-866-212-2272	Placing a request to access BabyBIG® Place a request for BabyBIG® via Health Canada's Special Access Programme (SAP). (See page 10 for more information). During regular work hours: Complete Special Access Request Form and fax to (613) 941-3194 After-hours, weekends & holidays: Call the SAP on-call officer at (613) 941-2108 (press 0) Speak with an on-call physician at the Infant Botulism Treatment and Prevention Program at the California Department of Public Health Anytime, 24 hours a day, 7 days a week: 1-510-231-7600

Step 2: Discuss specimen collection, transportation, and clinical presentation of the suspect case with the Botulism Reference Service for Canada.

During Regular Work Hours: **(613) 957-0902**

Make arrangements for transporting clinical and food specimens for laboratory analysis to the Botulism Reference Laboratory in Ottawa.

Step 3: Notify the local public health unit about suspect case of botulism without laboratory confirmation.

If food is suspected as the cause, the suspected source should also be reported.

Appendix 4: Important Telephone numbers

Ministry of Health

Office of the Chief Medical Officer of Health, Public Health

(416) 327-7392 During Regular Work Hours:
Monday to Friday (8:30 a.m. – 4:30 p.m.)

1- 866-212-2272 After-Hours, Weekends and Holidays

Health Canada

Botulism Reference Service Office

(613) 957-0902 During Regular Work Hours:
Monday to Friday (8:30 a.m. – 4:30 p.m.)

Special Access Programme

Fax Special Access Request Form A to (613) 941-3194
During Regular Work Hours: Monday to Friday (8:30 a.m. – 4:30 p.m.)
(613) 941-2108 (press 0) After-Hours, Weekends and Holidays

California Department of Public Health

Infant Botulism Treatment and Prevention Program

1-510-231-7600 Anytime, 24 hours a day, 7 days a week